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TITLE: A National Coordinating Center for Prehospital Trauma Research Funding Transfusion Using Stored Fresh Whole Blood

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14. ABSTRACT
This initial year of the project has been spent renewing all applications and space requirements, personnel changes, and associated protocol amendments. Initially the clinical study of this project was to include the Exception From Informed Consent (EFIC) and community consultation process with the plan well defined and approved by the local IRB. However, most significantly, in light of recent studies and a practice change in two other trauma centers, the study site Transfusion Committee has approved the administration of whole blood to male trauma patients as the standard of care. This changes the study to a Waiver of Informed Consent considerably advancing the start date for enrollment.

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Introduction:
The National Trauma Institute (NTI) proposed to utilize $499,995 in Joint Warfighter Medical Research Program Funding to extend the work previously completed looking at the use of fresh whole blood FWB) and its ability to be used for resuscitation. Hemorrhagic shock remains a major cause of potentially preventable death with common consequences including persistence and exacerbation of uncontrollable bleeding from refractory coagulopathy leading to early death from exsanguination. The Principal Investigator's preliminary data show that if whole blood is leukocyte reduced with a platelet sparing filter, it would be an acceptable standalone product for resuscitation from hemorrhagic shock that can be stored for prolonged periods of time. The aims for this funding are to 1) Determine the shelf life of whole blood units leukocyte reduced with a platelet sparing filter stored at 4 degrees; 2) prospectively determine the effectiveness of whole blood leukocyte reduced with a platelet sparing filter compared to component therapy as measured by coagulation capacity after transfusion and clinical outcomes; and 3) determine the feasibility of providing an inventory of whole blood leukoreduced with a platelet sparing filter for resuscitation of trauma patients in hemorrhagic shock.

Keywords:
Fresh Whole Blood; TEG; EFIC; resuscitation; platelets; leukoreduction, coagulation

Accomplishments:
The major goals of this project as identified in the Statement of Work are below with percent completion determinations and completion dates as appropriate.

Aims and Major Goals	Timeline in Months	Completion date	% Complete
Specific Aim 1: Determine the shelf life of whole blood Months			
Collection of whole blood units	1-9		0%
Testing of whole blood units for coagulation markers	1-9		0%
Analysis of in vitro study data	6-12		0%
Specific Aim 2: Determine the effectiveness of whole blood compared to component therapy			
Enrollment of trauma patients into the control arm, consisting of component therapy resuscitation	13-30		0%
Collection of whole blood units from volunteer blood donors	19-30		0%
Enrollment of trauma patients into the intervention group	19-30		0%
Blood sample collection from trauma patients	13-30		0%
Testing of blood samples from trauma patients	13-30		0%
Review of unexpected or adverse events by the medical monitor	13-30		0%
Data analysis	13-33		0%
Specific Aim 3: Determine the feasibility of providing whole blood for resuscitation of hemorrhagic shock			
Collection of data regarding whole blood utilization and cost	13-27		5%
Complete blood bank data base	28-30		5%
Analyze blood bank data base	28-33		0%
Other Major Tasks:			
Identification of communities in the UCLA catchment area	1-3		N/A
Advertisements for community meetings and focus groups	1-6		N/A
Hold community meetings and focus groups	3-6		N/A
IRB approval for Exemption from Informed Consent	4-9		N/A
Secretary General of the Army approval for Exemption from Informed Consent	7-18		N/A
Finalize consent form & human subjects protocol	10-12	10/08/2016	80%
Submit amendments, adverse events, and protocol deviations	As needed	10/08/2016	100%
IRB continuing review	Annually	11/09/2015	100%
Research group meeting	Quarterly	09/08/2016	100%

During this reporting period, the study PI has ensured that all regulatory/safety requirements were met, renewed the IRB application and certification of the laboratory space, and identified/delegated personnel to complete the project. There were some personnel changes due to individuals leaving the institution between the time the proposal was submitted and the time that funding was received. Earlier in the year meetings with the UCLA IRB were held to discuss the community consent plan for this study and as it turns out due to recent studies and the practice of two trauma centers transfusing whole blood to male trauma patients the community consultation plan and EFIC is no longer necessary. The UCLA Transfusion Committee has approved whole blood use at the study site as standard of care for male trauma patients. The most current protocol approved by the UCLA IRB and awaiting HRPO approval contains the above changes to the consent process.

All laboratory supplies to complete the clinical and laboratory portions of the study have been ordered and testing of the workflow to evaluate patients for coagulopathy in real-time is underway. The Blood Bank is working to identify a pool of whole blood donors and incorporating the new product (FWB) in terms of packaging and ordering/billing through the electronic health record. The study team is working with all disciplines involved in this study (Blood Bank, emergency Room, Trauma, Operating Room, Intensive Care Unit, etc) to coordinate and streamline standard operating procedures for the clinical portion of the study (aim 2). Study packets have been designed to minimize the impact on workflow in all patient locations. A secure database has been designed to store clinical research data and test data are being uploaded into the system and analyzed as a test of the procedure. Historical control data is currently being collected for comparison with prospectively-identified patients.

This project provides training for a research resident in clinical trial design and management as well as to training to student research assistants within the Emergency Medicine Research Associate program who will assist in identifying patients and collecting data.

At this stage of the project, there are no results to disseminate to communities of interest.

Plans for the next quarterly reporting period include receiving HRPO approval of the change in the protocol, receipt of the second TEG machine, initiation of Aim 1 activities (the determination of the shelf life of whole blood), and enrollment of patients is anticipated to begin. The Blood Bank anticipates the completion of identifying a pool of whole blood donors and initial collection in October 2016. Once that is complete, enrollment for aim 2, the clinical study, can begin.

Impact:
At this stage of the project, there has been no impact on the principal discipline, other disciplines, technology transfer, or society.

Changes/Problems:
The National Trauma Institute Science Committee reviewed this project during their quarterly meetings and recommended modifications to add strength to the already approved study. These recommendations were discussed with the PI and were implemented but prompted no change in the Statement of Work as approved by the DoD. There has been overall somewhat slow progress as the PI has not had a Research Resident; however, that has been remedied as of June 2016. The Science Committee discusses all studies in great detail and is heavily involved with the PI as to progression of studies.

In light of recent studies and the practice of two trauma centers transfusing whole blood to male trauma patients, the UCLA Transfusion Committee has approved whole blood use at the study site for male trauma patients. With this information, the UCLA IRB has approved a waiver of consent for the study addressing specific aim 2. This change from EFIC to Waiver of consent eliminates the need for the community consultation process and the appropriate tasks/milestones have been annotated as not applicable. This change will also significantly increase the speed at which the study can begin. This change in standard of care also changed the

protocol as only male patients will be enrolled in the interventional arm of the study and the women will provide the control arm. Men that are enrolled when whole blood is not available will also be part of the control group. These changes in protocol have been approved by the UCLA IRB and are awaiting approval by HRPO. Although these changes delay the initiation of the study they do serve to increase the speed at which the Aim 2 specifically can be started overall as the community consultation process which can easily take several months does not have to be completed and the study protocol does not need Secretary of the Army signature which generally takes another six to nine months.

As part of protocol development, initial review from the DoD, and the PI's analysis of preliminary work platelet mapping was added as an end point for Aim 2. To achieve platelet mapping, the most direct measure of the contribution of platelets to clotting, a second TEG machine is necessary. There is no increase to the overall budget.

Based upon the above changes in practice and subsequently the protocol essentially the work to achieve all three Specific Aims can be performed concurrently.

Products:
There have been no products as a result of this project at this time.

Participants:

Name	Project Role	Nearest person month worked	% Effort	Contribution to the project
Donald Jenkins	Principal Investigator	0.6	5%	Oversight of entire project
Roy Estrada	Program Manager	0.96	8%	Regulatory oversight and coordination of regulatory reviews and reporting
Monica Phillips	Research Operations Director	0.24	2%	Negotiated and executed subaward.

There are no changes in the active other support for the PI or key personnel.

The University of California Los Angeles is collaborating and actually performing the study. They are a subaward recipient to this grant.

Special Reporting:
Quad Chart: The Quad Chart for this grant is attached as appendix A.